52. (Amended) A compound according to claim 50, wherein $C_a$ is –NH-$(CH_2)_n$-C(O)-, wherein n is an integer between 1 and 25.

53. (Amended) A compound according to claim 52, wherein $C_a$ is –NH-$(CH_2)_5$-C(O)-.

54. (Amended) A compound according to claim 52, wherein $C_a$ is –NH-$CH_2$-C(O)-.

55. (Reiterated) A compound selected from the group consisting of biotin-S-Ph-C(O)-F*l*YEE-$NH_2$, biotin-OPh-C(O)-F*l*YEE-$NH_2$, LC-biotin-S-Ph-C(O)-F*l*YEE-$NH_2$ , biotin-Gly-OPh-C(O)-F*l*YEE-$NH_2$, fluorescein-Gly-OPh-F*l*YEE-$NH_2$, LC-biotin-OPh-C(O)-F*l*YEE-$NH_2$, argatroban-$AEA_3$-βAla-Gly-OPh-C(O)-F*l*YEE-$NH_2$, and fluorescein-thiourea-$AEA_3$-Gly-OPh-C(O)-F*l*YEE-$NH_2$.

Please CANCEL Claims 56-57.

Please ADD the following new claim.

58. (NEW) A compound as claimed in claim 1, wherein the target molecule comprises human serum albumin, and the affinity group A comprises a sequence of amino acid residues -$O_1$-$O_2$-$X_1$-$X_2$-B- wherein the amino acid residues are independently selected from the group consisting of all twenty naturally occurring amino acids in either L or D configuration.

## REMARKS

Upon entry of the instant amendments, claims 1-2, 4-35, 40-55 and 58 will be pending. Claims 3, 36-39 and 56-57 have been canceled. Claims 1-2, 4-6, 9-19, 21-22, 24, 27-28, 30-35, 40-54 have been amended. Claim 58 is newly added.

These claims have been reviewed in detail and all the amendments made therein find proper support in the specification as outlined below.

- Claim 1 has been amended by

  o indicating that the presence of first and second connecting groups Ca and Cb is optional, as supported by page 7 lines 22-26 and page 16 lines 13-16 of the description; and

  o defining the affinity group in accordance with the definition provided in page 5 lines 20-21 of the description;

- New claim 58 has been introduced. The subject matter of this claim comprises mainly the subject canceled from former claim 1, i.e., that the target molecule is HSA (see page 6 lines 17-20 of the description) and that the affinity group comprises a sequence of amino acid residues -O1-O2-X1-X2-B- (see page 14 lines 21-24 of the description);

- Claim 2 has been rendered dependent on claim 58 and glutamic acid has been inserted in the definition of O1, as supported by page 8 line 9 of the description as filed, and also to provided antecedent to original claim 12;

- Claim 3 has been canceled;

- The dependency of claims 4-6 and 9-19 has been changed;

- Claims 7, 8 and 20 remain the same;

- Claim 21 has been clarified and thioamine and amides have been inserted in the definition of the functional group, as supported by page 10 lines 1-6 of the description;

- Claim 22 has also been clarified to avoid any confusion;

- Claims 23, 25, 26 and 29 remain unchanged;

- Claims 24, 27, 30-32 have been clarified, and the subject matter of claims 31 and 32 has been inserted in page 16 of the description to provide support therefor;

- Claim 28 has been amended by removing the substituents that were inappropriate, i.e., those containing R, R2 or R3 therein. The phenyl substituents of this claim have also been inserted in page 10 line 21 of the description to provide support therefor;

- Claims 33-35 have been clarified;

- Claims 36-39 have been canceled;

- Claims 40-42 have been clarified, and the subject matter of claims 41-42 has been inserted in page 16 of the description to provide support therefor;

- Claims 43-55 have been clarified. With respect to the amendment made to claim 46, support for this amendment can be found in page 7 line 29 of the description; and

- Claims 56-57 have been cancelled.

None of these amendments introduce new matter, and in fact have been made to better define the invention and bring the claims and the specification in conformity with each other. The claim amendments have not been made for purposes related to patentability. Early and favorable action is requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket no. **500862000700**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: May 9, 2002

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Specification:**

Paragraph beginning at Page 10, Line 13 has been amended as follows:

In one embodiment of the invention, the reactive group has the formula $-X-R_1-C(O)-$, where X is sulfur, oxygen, or nitrogen; $R_1$ includes a substituted or unsubstituted aromatic group; and C(O) represents a carboxyl group. Also suitable is a reactive group of the formula $-X-R_1-C(S)-$, where X is sulfur, oxygen, or nitrogen; $R_1$ includes a substituted or unsubstituted aromatic group; and C(S) is a thiocarbonyl group. Preferably, X is sulfur or oxygen. In another preferred embodiment, X is directly bonded to an aromatic carbon in the $R_1$ group. In a more preferred embodiment, $R_1$ is a substituted or, preferably, an unsubstituted phenyl. In this context, by "substituted phenyl", we mean a phenyl group bearing substituents such as halogen, NO2, SO2NH2, SO2NHF, CF3, CCl3, CBr3, C=N, SO3H, CO2H, CHO, NHR, OH, NHCOCH3, OCH3, CH3, and CH2CH3, in addition to the –X- and –C(O)- groups explicitly laid out in the formula. In a more preferred embodiment, $R_1$ is unsubstituted phenyl and the –X- and –C(O)- substituents are bonded to the phenyl group in a para configuration. In another preferred embodiment of the invention, the reactive group carboxyl group is directly bonded to the $O_1$ amino acid of the affinity group, generating a stable amide bond.

Paragraph beginning at Page 16, Line 21 has been amended as follows:

For the most part, the connector(s) will be bifunctional, about 1-20 atoms in length, which atoms may be carbon, nitrogen, oxygen, sulfur, phosphorus, and the like. The connector(s) may be alkylene groups, generally of from 2-16, more usually of from 1-25, carbon atoms, polyoxyalkylene groups, where the alkylene groups will be of 2-3 carbon atoms, and having from 1-8, more usually of from about 1-6, units, an amino acid, including alpha and omega amino acids, or oligopeptide having from 1-8, usually 1-6, amino acids, where the amino acids may be polar or non-polar, charged or uncharged, aliphatic, alicyclic, aromatic or heterocyclic, naturally occurring or synthetic. The connector(s) may also have the structure of an affinity group as described above, thereby providing additional binding affinity at the target site. In a preferred embodiment, Cb is bonded to the reactive group via an ester, thioester, amide, sulfonate ester or sulfonamide linkage. In a further preferred embodiment, Cb is bonded to the O1 amino acid residue in the affinity group via an ester, thioester, amide, sulfonamide, urea, thiourea or carbamate linkage. In a further preferred embodiment, Ca is bonded to E by an ester, thioester, amide, sulfonate ester or sulfonamide linkage. In a further preferred embodiment, Ca is bonded to the reactive group by an ester, thioester, amide or sulfonate ester linkage.

**In the Claims:**

1. (Amended) A compound [according to the] of formula E-$C_a$-R-$C_b$-A, wherein E is a therapeutic or diagnostic agent, R is a reactive group, $C[_a]_b$ and $C[_b]_a$ are optional first and second connecting [connector groups between E and R and between R and A,] respectively, and A is an affinity group comprising any molecule or part of a molecule possessing specific binding determinants for a target molecule having an affinity for human serum albumin, wherein affinity group A comprises a sequence of amino acid residues -$O_1$-$O_2$-$X_1$-$X_2$-B in which the amino acid residues are independently selected from the group of all twenty naturally occurring amino acids.

2. (Amended) A compound according to claim [1] 58, wherein [affinity group A comprises the sequence $O_1O_2X_1X_2$ B wherein:] amino acid residue $O_1$ is selected from the group consisting of phenylalanine, arginine, glutamine, tyrosine, glutamic acid and tryptophan; amino acid residue $O_2$ is selected from the group consisting of leucine, arginine, glutamic acid, tryptophan and phenylalanine; amino acid residue $X_1$ is selected from the group consisting of phenylalanine, tryptophan, methionine and tyrosine; amino acid residue $X_2$ is selected from the group consisting of serine, arginine and glutamic acid; and amino acid residue B is selected from the group consisting of serine, arginine and glutamic acid.

4. (Amended) A compound according to claim [2] 58, wherein one of the five amino acid residues is an L amino acid residue and the other four amino acid residues are D amino acid residues.

5. (Amended) A compound according to claim [3]2, wherein the L-amino acid residue is selected from the group consisting of the amino acid residue $O_2$, the amino acid residue $X_1$, and the amino acid residue $X_2$.

6. (Amended) A compound according to claim [2]58, wherein one of the five amino acid residues is a D-amino acid residue and the other four amino acid residues are L-amino acid residues.

9. (Amended) A compound according to claim [2]58, wherein $O_1$ is phenylalanine and $O_2$ is leucine.

10. (Amended) A compound according to claim [2]58, wherein $O_1$ is arginine and $O_2$ is arginine.

11. (Amended) A compound according to claim [2]58, wherein $O_1$ is glutamine and $O_2$ is glutamic acid.

12. (Amended) A compound according to claim [2]58, wherein $O_1$ is glutamic acid and $O_2$ is tryptophan.

13. (Amended) A compound according to claim [2]58, wherein $O_1$ is tryptophan and $O_2$ is tryptophan.

14. (Amended) A compound according to claim [2]58, wherein $O_1$ is tryptophan and $O_2$ is glutamic acid.

15. (Amended) A compound according to claim [2]58, wherein $X_1$ is tyrosine.

16. (Amended) A compound according to claim [2]58, wherein $X_2$ is glutamic acid.

17. (Amended) A compound according to claim [2]58, wherein B is glutamic acid.

18. (Amended) A compound according to claim [2]58, wherein $O_1$ is phenylalanine, $O_2$ is D-leucine, $X_1$ is tyrosine, $X_2$ is glutamic acid, and B is glutamic acid.

19. (Amended) A compound according to claim [2]58, wherein the amino acid residue B is a C-terminal amino acid residue.

21. (Amended) A compound according to claim [2]58, wherein [the compound further includes a reactive group attached to the affinity group, and wherein] the reactive group [includes] comprises a functional group selected from the group consisting of carboxy, phosphoryl, alkyl esters, thioesters, phosphoesters, ortho esters, imidates, mixed anhydrides, amides, thioamine and disulphides.

22. (Amended) A compound according to claim 21, wherein $C_b$ is absent and the reactive group is bonded directly to the $O_1$ amino acid residue in the affinity group.

24. (Amended) A compound according to claim 21, wherein the reactive group has the formula $-X-R_1-C(O)-$, wherein [C(O) is an alpha carboxyl,] $R_1$ [includes] comprises a substituted or unsubstituted aromatic group and X is selected from the group consisting of S, O and N.

27. (Amended) A compound according to claim 26, wherein [the] -X- and -C(O)- [substituents] are bonded to the [unsubstituted] phenyl [is] in a para configuration.

28. (Amended) A compound according to claim 24, wherein $R_1$ is phenyl substituted with one or more groups selected from the group consisting of a halogen, $NO_2$, [$SO_2NR_2$, $SO_3R$,] $SO_2NH_2$, $SO_2NHF$, [$NR_3^+$,] $CF_3$, $CCl_3$, $CBr_3$, C≡N, $SO_3H$, $CO_2H$, [$CO_2R$,]CHO, [$CORNH_2$, NHR, $NR_2$,] OH, $NHCOCH_3$, [NHCOR,] $OCH_3$, [OR,] $CH_3$, and $CH_2CH_3$ [and $RC_6H_5$].

30. (Amended) A compound according to claim 21[further comprising a first connecting group connecting the reactive group and the affinity group] wherein $C_b$ is present.

31. (Amended) A compound according to claim [30]28, wherein [the first connecting group] $C_b$ is bonded to the reactive group via an ester, thioester, amide, sulfonate ester or sulfonamide linkage.

32. (Amended) A compound according to claim 30, wherein [the first connecting group] $C_b$ is bonded to the $O_l$ amino acid residue in the affinity group via an ester, thioester, amide, sulfonamide, urea, thiourea or carbamate linkage.

33. (Amended) A compound according to claim 30, wherein $C_b$ [the first connecting group includes] comprises a backbone chain of between about 1 and about 25 atoms.

34. (Amended) A compound according to claim 33, wherein $C_b$ [the first connecting group includes] comprises a backbone chain of between about 2 and about 16 carbon atoms.

35. (Amended) A compound according to claim 30, wherein $C_b$ [the first connecting group includes]comprises an unsaturated carbon atom backbone chain of between about 1 and about 25 atoms.

40. (Amended) A compound according to claim [36]58 [further comprising a second connecting group connecting the entity to the reactive group] wherein $C_a$ is present.

41. (Amended) A compound according to claim 40, wherein $C_a$ [the second connecting group] is bonded to E [the entity] by an ester, thioester, amide, sulfonate ester or sulfonamide linkage.

42. (Amended) A compound according to claim 40, wherein $C_a$ [the second connecting group] is bonded to the reactive group by an ester, thioester, amide or sulfonate ester linkage.

43. (Amended) A compound according to claim 40, wherein $C_a$ [the second connecting group includes] comprises a backbone chain of between about 1 and about 25 atoms.

44. (Amended) A compound according to claim 43, wherein $C_a$ [the second connecting group includes] comprises a backbone chain of between about 2 and about 16 carbon atoms.

45. (Amended) A compound according to claim 40, wherein $C_a$ [the second connecting group includes] comprises an unsaturated carbon atom backbone chain of between about 1 and about 25 atoms.

46. (Amended) A compound according to claim [36]1, wherein the[entity comprises a biotinyl group] diagnostic agent comprises biotin.

47. (Amended) A compound according to claim 46, wherein [the biotinyl group] biotin is bonded directly to the reactive group by an ester, thioester or amide linkage.

48. (Amended) A compound according to claim 46, wherein the reactive group has the formula –X-Ph-C(O)-, and wherein X is oxygen, sulfur or nitrogen.

49. (Amended) A compound according to claim 48, wherein the –X- and –C(O)- [substituents] on the [Ph] phenyl group are bonded [is]in a para configuration.

50. (Amended) A compound according to claim 47, [further comprising a second connecting group connecting the biotin group to the reactive group] wherein $C_a$ is present.

51. (Amended) A compound according to claim 50, wherein $C_a$ [the second connecting group]is bonded to the biotin group by an amide linkage.

52. (Amended) A compound according to claim 50, wherein $C_a$ [the second connecting group] is $–NH-(CH_2)_n-C(O)-$, wherein n is an integer between 1 and 25.

53. (Amended) A compound according to claim 52, wherein $C_a$ [the second connecting group]is $–NH-(CH_2)_5-C(O)-$.

54. (Amended) A compound according to claim 52, wherein $C_a$ [the second connecting group]is $–NH-CH_2-C(O)-$.

58. (NEW) A compound as claimed in claim 1, wherein the target molecule comprises human serum albumin, and the affinity group A comprises a sequence of amino acid residues $-O_1-O_2-X_1-X_2-B-$ wherein the amino acid residues are independently selected from the group consisting of all twenty naturally occurring amino acids in either L or D configuration.